Question to the Board: Department of Defense Role in Development of New Antimicrobial Agents

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Problem Statement

Current convergence of circumstances*

- **High levels of antibiotic resistance among important pathogens**
- **Uneven supply of novel classes of antibiotics**
  - **Few new drugs in "pipeline"**
- **Dramatic reduction in number of pharmaceutical companies engaged in anti-infective drug discovery and development**

Wenzel, R.P. The antibiotic pipeline-challenges, costs, and
NEJM 351(6): 523-6, August 5, 2004

Antimicrobial Resistance

- Fleming discovers penicillin in 1928- beginning of antibiotic era
- Late 1940's, early 1950's emergence of β-lactamase-producing bacteria resistant to penicillin
- 1970's-80's emergence of methicillin-resistant *Staphylococcus aureus* (MRSA)
- Today in the US
  - Half of community-acquired *Streptococcus pneumonia* isolates are resistant to penicillin
  - Half of SA isolates in hospitals are MR
  - One-third of enterococci isolates in hospitals are resistant to vancomycin

Decreased Deployment of Novel Antibiotics

- **Limited number of types of anti-infective drugs**
  - **1930's-1940's (β-lactams, sulfonamides, aminoglycosides, chloramphenicol)**
  - **1950's-1960's (tetracycline, macrolides, glycopeptides, rifamycins, quinolones, and trimethoprim)**
  - **1970's -1990's ???**
  - **2000- (oxazolidinones, cyclic lipopeptides)**

Anti-infectives: Risky Business

- Risk-adjusted net present value (NPV_R)
  - (return in future $ [millions] after adjustment for investment and lost income)
  - Does not include risk of failure, time, and other direct and indirect costs (opportunity costs)
- Estimated NPV_R's
  - Antibiotics: 100
  - Cancer therapy: 300
  - Neurologic: 720
  - Musculoskeletal: 1150
- Since mid-1980's, fewer pharmaceutical firms investing in anti-infective drugs

...in the year 2002, something like 400 new pharmaceutical agents were licensed by the FDA...In that year there were no genuinely new antibiotics among them...that's a striking thing...

Dr. W. Schaffner,
Vanderbilt Medical Center,
CBS News "60 Minutes"
May 2, 2004

Army Question for the Board 14 May 04

1. **The US military medical research portfolio excludes development of novel antibiotics to treat infections caused by drug-resistant organisms.**

2. **Infections caused by these organisms are affecting military personnel in current operations.**

- ***Request the Board review the issue of emerging antibiotic-resistant microbes, and***
- ***Recommend the role for the military medical research community in the development of new antibiotics to treat infections caused by resistant organisms.***